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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,560	02/06/2001	Curtis R. Brandt	032026-0460	8196

23524 7590 06/08/2007

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/777,560	BRANDT ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-35* is/are pending in the application.

4a) Of the above claim(s) *32-35* is/are withdrawn from consideration.

5)☒ Claim(s) *23-27* is/are allowed.

6)☒ Claim(s) *28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 18, 2007 has been entered. Claims 23-31 are newly presented and under examination. Newly presented claims 32-35 are withdrawn from consideration being drawn to non-elected subject matter.

2. The rejection of claims 11-13 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the entire scope of the claimed invention, is moot in view of the cancellation of claims 11-13.

Claim Rejections - 35 USC § 112

3. Claims 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an antiviral peptide that treats herpes simplex virus (HSV) type 1 ocular disease, does not reasonably provide enablement for a composition comprising an antiviral peptide that treats HSV-1 oral or genital manifestations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement

and whether any necessary experimentation is "undue." These factors include, but are not limited to the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims is unreasonable, encompassing the treatment and inhibition of HSV-1, which has ocular, oral and genital manifestations. The nature of the invention is the treatment or inhibition of the HSV-1 virus; the antiviral peptide may interact with the virus components, although the exact mechanism is not known/disclosed (page 17, lines 15-17). The amount of direction provided by the inventor in the specification does not adequately enable one of skill in the art to use the antiviral peptide of SEQ ID NO: 1 to treat (improve) HSV-1 oral or genital disease. The working examples are clearly directed to HSV-1, a member of the enveloped viruses, in its ocular manifestation. With regard to HSV-1 ocular disease, the specification demonstrates that SEQ ID NO: 1 (EB and EBX peptides, Table 1) is capable of inhibiting HSV-1 infection in Vero cells in plaque assays (see Figures). Applicant has shown that SEQ ID NO: 1 with NH_2 or a biotin-aminohexanoyl groups at the amino terminus had an inhibitory effect on the progression of ocular disease in mice (Figure 9). This amount of guidance is not adequate to enable one of skill to treat or inhibit oral or genital manifestations in warm-blooded animals, even humans. A composition that treats HSV-1 must impart therapeutic benefit to the recipient. Applicant's specification does not lead one to expect that the claimed peptides will treat human HSV-1 oral or genital disease in humans. The prior art supports a treatment and protection against recurrent mouse ocular disease (Richards *et al.*, *Journal of*

Virology, 2003, 77(12):6692-6699, "Richards", or record). Richards teaches that prevention of primary infection is difficult because HSV-1 is often acquired very early in life and becomes a latent infection (page 6692, column 1). Attempts to vaccinate and treat ocular disease have been disappointing, given that a promising candidate agent reduced viral shedding but failed to reduce the incidence of the disease. Subunit vaccines have also failed because of the complex nature of the virus and the need for a vaccine to modulate the nature of the body's immune response to the virus (page 6692, second column), demonstrating a lack of predictability in the art. Richards immunized mice (reactivated latent infection) with HSV-1 glycoproteins intranasally and observed protective immunity against recurrent episodes, and in cases where clinical symptoms developed, the treated mice recovered faster (pages 6696-6697, bridging paragraph).

In view of the unreasonable breadth of the claims, the nature of the invention, the state of the prior art, the high level of one of ordinary skill, the low level of predictability in the art, the limited amount of direction provided by the inventor, the limited working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, the claims are not enabled for their full scope.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the treatment of viral infections caused by HSV are fully enabled by the data presented in the application and confirmed by the supplemental results set forth in the Brandt Declaration and USPGPUB 2005/0203024 submitted with and discussed in the response filed May 6, 2006.

In response to Applicant's remarks, the Office has considered Applicant's response and the Brandt declaration filed May 6, 2006. Applicant points to Example 2, Figures 1A-1E, and

Table 3 as evidence that the claimed peptides show significant antiviral activity against HSV-1 *in vitro*. Example 9 demonstrates *in vivo* activity by the claimed peptides; inhibition of the progression of ocular disease in mice as judged by vascularization and stromal keratitis. Applicant presents new evidence in the declaration of Dr. Curtis R. Brandt, co-inventor, filed under 37 CFR 1.132 on May 5, 2006. The evidence presented in the declaration relates to U.S. Patent Application Publication 2005/0203024 (same inventorship) and to Examples A-E of the declaration appendix. The summary of the evidence presented that directly relates to elected SEQ ID NO: 1 is that SEQ ID NO: 1 blocked infection by Influenza A and H5N1 *in vitro*, and SEQ ID NO: 1 protected mice infected with lethal doses of Influenza PR8 from death both pre- and post-infection. SEQ ID NO: 1 is capable of reducing viral titers of vaccinia virus in vitro in a dose-dependent manner. SEQ ID NO: 1 is also capable of inhibiting infection of cells *in vitro* by HPV-31 and BPV-1.

In response, the Office has considered the declaration of Dr. Curtis Brandt, along with the evidence submitted therewith, however, the declaration is insufficient to overcome the rejection. It is clear from the evidence that SEQ ID NO: 1 is capable of interacting with enveloped viruses Influenza, HSV-1, HPV-31 and BPV-1, for example. While Applicant has provided some in vivo data in mice for HSV-1 ocular disease and influenza, there is a lack of *in vitro* data for HSV-1 oral and genital manifestations. Richards teaches that prevention of primary infection is difficult because HSV-1 is often acquired very early in life and becomes a latent infection (page 6692, column 1). Attempts to vaccinate and treat ocular disease have been disappointing, given that a promising candidate agent reduced viral shedding but failed to reduce the incidence of the disease. Applicant has not overcome these serious obstacles. The specification does not teach

one of skill in the art how to deal with the latency aspect of HSV-1. A patient with latent HSV-1 infection does not have viral particles for the claimed peptide to act on. In this case, the patient will not be treated for HSV-1 infection.

In their previous response, Applicant pointed to Brandt *et al.* (*Antimicrobial Agents and Chemotherapy*, 1996) and Brandt *et al.* (*J. Virological Methods*, 1992, 36:209-222) as evidence that agents which are active in the mouse model are typically active in other models of HSV. The Office has considered the teachings of Brandt *et al.* (*Antimicrobial Agents and Chemotherapy*, 1996), which state that the mouse model for HSV-1 ocular disease and the rabbit model for HSV-1 ocular disease responded to treatment with idoxuridine and TFT, indicating that they are equivalent models. The teachings of Brandt *et al.* (*J. Virological Methods*, 1992, 36:209-222) have not been considered because this article could not be found attached to the response of May 5, 2006, or any other information disclosure submission prior to or after the May 5, 2006 response.

The ability of the claimed antiviral peptide to treat ocular disease HSV-1 has been established. However, the ability of the claimed peptide to treat other HSV-1 manifestations has not been established in any animal model. In order for claims to a composition that improves HSV-1 oral and genital disease in humans, there must be evidence, given the latency of the virus. Evidence relating to one virus (HSV-1) in one manifestation (ocular disease) does not correlate to all other diseases, such as oral or genital herpes. Therefore, the rejection is maintained for reasons of record.

Conclusion

5. Claims 23-27 are allowable. Applicant's request for rejoinder of non-elected subject matter (claims 32-35) is not appropriate at this point in prosecution since the elected invention remains rejected under 35 U.S.C. 112, first paragraph. Although claims 32-35 depend from allowable claims 23 and 24, the elected invention as a whole (includes claims 28-30) remains rejected.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 6-4-2007
Primary Examiner, TC1600